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TWO CASES OF MALIGNANT OR ULCERATIVE ENDOCARDITIS.

A CLINICAL LECTURE DELIVERED AT THE PHILADELPHIA
HOSPITAL,

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pital.*

I HAVE here some specimens showing the lesions of malignant or ulcerative endocarditis as seen in a case recently in the wards of the hospital, and also some photographs of a case which came to my notice in the Presbyterian Hospital some time ago. I also have here the specimens from the latter case, and shall demonstrate to you as well as I can, the pathological lesions. In this heart there are seen on the leaflets of the mitral valve, a fringe of soft vegetations which were very friable when first removed, and in fact still are easily broken. They project into the ventricle and auricle, interfering seriously with the circulation. They are also seen on the aortic valves, and in this instance we find the rather rare occurrence of the lesions on the tricuspid and pulmonary valves. On microscopical examination of a teased preparation, these larger masses seemed to be made up of a granular substance in which were innumerable micrococci. In addition to this hyaline structureless appearance of the mass, a croupous or fibrinous exudation, cell proliferation was seen, with leucocytes in large numbers. The micrococci not only invested the proliferating membrane, but also dipped deeply into the lymph spaces of the neighboring structures looking not unlike the penetrating pegs of epithelioma. The smaller masses were less free from granular material and contained more of the cellular structure, and showed

especially, old connective tissue elements most markedly. These proliferating structures while to a certain extent limited to the valves, are in this case also seen on the chordæ tendineæ, and on the wall of the heart itself, budding out from the endocardium.

In cases of malignant or ulcerative endocarditis, not only do we find these proliferative masses, but quite frequently we also find ulcerations with or without fungoid growths of inflammatory material. These ulcerations are found in the valve and in the heart muscle, and may lead to perforation. Microscopical examination of such ulcers shows abundant micrococci and the presence of round cells and granulation tissue. The ulceration may perforate the valve or the heart muscle itself, and lead to the development of aneurism, or to leakage from one cavity to another, or from the cavity of the heart into the pericardium, causing a fatal result. In addition to the fungous growths and these ulcerations, there are found in some instances, minute abscesses. The pus in these abscesses contains an abundance of micrococci.

In this second specimen the mitral valve is affected alone. The enormous degree of proliferation of the new growth can be readily seen. That on the anterior leaflet of the mitral valve projects into the ventricle, while that on the posterior leaflet projects into the auricle.

The presence of this granular material and the existence of micrococci in the new growths, would of necessity lead us to infer that the blood was infected, and such is the case. Microscopical examination shows abundance of micrococci floating free in the blood, and some are also found in the leucocytes. The infection of the blood and the presence of micrococci in these free situations where they can be readily disturbed by the blood current, lead us to expect structural changes in the peripheral circulation. By the force of the blood

current, micrococci, cells and granular debris are carried into the distal circulation and form infarcts. When the disease is on the left side of the heart, these infarcts are seen in almost all parts of the arterial circulation; for instance, in the case recently under observation, there were innumerable infarcts in the skin, and nearly all the internal organs. Microscopical examination would show in addition to the hæmorrhage of the infarct, the presence of micrococci, occluding some minor capillary. The mucous membrane and the serous membranes may also be similarly affected in these cases. In this instance, infarcts were seen in the peritoneum and in the pericardium over the surface of the heart. The mucous membrane of the gastro-intestinal tract, showed numerous infarcts. The nature of these infarcts depends largely upon the nature of the primary infecting material. If there is an abundance of pus, they rapidly change into abscesses. In other instances, they remain as simple hæmorrhagic infarcts, and if the patient lives, undergo the changes usually seen after emboli. Here is a section of the intestine which shows the hæmorrhages in the mucous membrane. In this case, the most remarkable lesions were the number and extent of the infarcts in the stomach, particularly toward the cardiac end. In the first case, the only infarcts found were in the kidneys. There was also most marked glomerulo-nephritis. In the second case, the renal infarcts were not so large, but there were innumerable small ones in the capsule of the kidney, and microscopical examination would in all probability reveal the evidences of glomerulo-nephritis. The spleen, you observe, shows the infarcts very distinctly.

Not only are the lesions found in these structures, but capillary emboli may also occur in the brain. And not alone are the capillaries involved, but large plugs may be broken off and carried into the cerebral

arteries, cutting off the circulation of a large portion of the brain structure producing hemiplegia and other grave cerebral symptoms. In the second case, a large thrombus had formed in the iliac artery, with obstruction to the blood supply of the lower extremity. It was evidently a recent formation, as it had produced no symptoms during life.

In addition to these changes which are noted in most cases of malignant endocarditis, namely, the changes in the structure of the valves; of the endocardium and of the heart muscle and changes in the blood, and secondarily, the presence of emboli and infarcts throughout the arterial circulation, there are often other lesions. For instance, in many cases the lesions of rheumatism or pneumonia or diphtheria are present. In other cases there are found in some portion of the body small abscesses, disease of the bones or some suppurative process. In such cases the endocarditis is secondary to the disease in the peripheral structures. Many cases, for instance, have been reported in which a pelvic abscess had been the primary origin of the disease. In the same way, in disease of the bone and in rapidly growing cancer which has undergone inflammatory changes, malignant endocarditis may develop.

These anatomical conditions have led to the division of the disease into three classes: First, those cases in which there are present only lesions of the heart and of the blood, and lesions due to emboli, are classed as cases of idiopathic or spontaneous malignant endocarditis; Second, those cases in which the lesions of rheumatism or pneumonia are found in addition, are classified simply as cases of associated malignant endocarditis; Third, those cases in which the disease is due to the presence of suppurative inflammation in the distal circulation or to a general septic process, are classified as cases of secondary malignant endocarditis.

By the knowledge of the anatomical characters of the disease, one can readily trace and keep well in mind the clinical history of these cases. First, from the fact that micrococci are found in the blood and in the inflamed structures, we should infer that there must be some general symptoms due to the septic process, and such is eminently the case. Second, the severe local cardiac lesion produces symptoms characteristic of obstruction in the orifices, while finally, the character of the primary lesion determines the presence and nature of the third class of symptoms, namely, those arising from peripheral infarcts and inflammations.

Cases of malignant endocarditis are characterized by rigors, irregular fevers and sweats, and by the occurrence in the later stages, of jaundice due to disorganization of the blood. There may also be vomiting and diarrhœa which examination shows is not dependent upon organic lesions of the stomach and bowels, but on the septic process. Enlargement of the spleen, another accompaniment of the septic process is also observed. The affection is sometimes accompanied by inflammation of the serous membranes, especially of the brain. Indeed, the only prominent symptoms of malignant endocarditis may be cerebral.

From the blood lesions, depending upon the extent to which the blood has become disordered and infected with the micrococci, and secondarily, upon the reaction of the structures to the micrococci in the blood, we have different types of the disease. Clinical experience has led us to divide the cases into four classes, the pyæmic, the typhoid, the cerebral and the cardiac. The pyæmic type, as its name indicates, resembles pyæmia in its symptoms and course. The cerebral type simulates inflammation of the meninges of the brain in its symptoms. Possibly without any symptoms referable to the heart, there will be pain in

the head and in the back of the neck, with high fever, drowsiness, stupor, convulsions and coma. In the typhoid type, the symptoms simulate those of typhoid fever in many respects, the affection beginning with irregular chills, irregular fever, and being accompanied by profuse perspiration, emaciation, low muttering delirium, a dry, brown tongue, and even the occurrence of diarrhœa. In the cardiac form of the disease, the symptoms depend not so much upon the condition of the blood, as upon the primary cardiac lesions. While a healthy heart may undergo the changes which I have demonstrated to you, a diseased heart is much more likely to do so. In many cases of cardiac disease, the diseased structures seem to furnish a hot-bed for the development of the micrococci. More cases of malignant endocarditis are found in old cases of cardiac disease than in any other class. In the cardiac type, we have in addition to the symptoms referable to the heart, namely, dyspnœa, pain and distress about the præcordia, and palpitation,—also irregular fever and sweats.

The local symptoms due to the presence of this severe and extensive inflammation of the cardiac structure are pronounced and distressing. From the appearance of this enormous outgrowth on the mitral valve (second case), you can infer considerable obstruction to the blood-current, and hence the production of a murmur. So, in all cases, a murmur is heard at the orifice affected. Sometimes it is heard at several points, according to the diverse seat of the lesion. The murmur is usually strong and low in pitch. It may be systolic or diastolic. It is conducted or transmitted in accordance with the laws that govern murmurs, but differs in the variation of its character. From time to time it may be high or low pitched, loud or soft, strong or feeble, indeed, may temporarily disappear, such changes depending on the change of the

outgrowths by loosening and floating off in the bloodstream. With the murmur, would arise other evidence of obstruction, such as dilatation of one or more of the chambers of the heart, with increase in the area of dullness and of impulse. Under these circumstances, the heart acts more violently, is likely to be irregular and very frequent, while palpitation and cardiac dyspnoea would be present.

Finally, we look to the nature of the central lesion for the character of the symptoms developed in the peripheral circulation. If largely purulent in character, the infarcts would rapidly be converted into abscesses. In most instances, simple hæmorrhagic infarcts are observed. In both, crococi abound.

The infarcts or capillary hæmorrhages are observed in the skin, the conjunctivæ, and the external mucous membranes. They are seen in the retina, and their presence in the gastro-intestinal or urinary tracts may be inferred from the occurrence of blood in the natural discharges, or of hæmorrhages from these localities. Their presence in the brain is determined by the phenomena common to cerebral emboli. In the skin, these infarcts are most abundant, and are distinguished by their bright red color and their persistence on pressure.

The case from which the first specimens were removed was a typical example of malignant endocarditis, and I shall ask your attention to the prominent points in its history: W. J.,¹ white, was admitted to the medical wards of the Presbyterian Hospital, October 3, 1884, suffering with rheumatism, localized in the left knee and the right shoulder and elbow. He stated that he had been feeling badly for some time, and had been losing flesh and strength. Previous to the recent illness he had had small-pox, syphilis, and gonorrhœa. The fever was very high, and out of proportion to the

¹ See Transactions College of Physicians of Philadelphia, 1886.

local symptoms. It was irregular, and at times there were profuse, exhausting sweats. This case was typical in its marked remissions and intermissions, the temperature sometimes going as high as 105° , and on one occasion, going as low as 96.5° . Some time after admission, the patient complained of pain about the præcordia, and, on examination, a murmur at the mitral valve was found. No particular stress was laid upon the cardiac trouble, which was regarded as a simple endocarditis, which often arises in the course of rheumatism. During the course of the rheumatism, he had, one month after admission, an attack of pneumonia of the lower lobe of the right lung. The fever continued and the exhaustion became extreme, and finally, one day, after a chill, congestion of the lungs took place, and death resulted. The duration of the illness was sixty-eight days.

An interesting feature of this case was the development of malignant endocarditis in the course of rheumatism, and the occurrence, during the disease, of pneumonia.

Pneumonia is often a primary affection in this disease. Moreover, in those cases in which the right heart is affected, an infarct may form in the lung, causing pulmonary apoplexy and associate pneumonia, and such was possible in this case. Otherwise, it is not liable to complicate endocarditis.

The irregular fever, the exhaustive sweats, and the diarrhœa due to sepsis were marked. The cardiac murmur and the dyspnœa caused by the local lesion were present, but the occurrence of infarcts was not demonstrated during life. Such is a summary of the interesting clinical features observed.

The case from which the second specimens were removed was N. S., aged twenty-seven years, a German, who was admitted to my wards in this hospital, August 26, 1886. At the same time, her husband and

children were admitted suffering with some febrile complaint, thought to be malarial. This is important, as indicating that the family were in straitened circumstances, and probably living in an unhealthy locality. The patient had been ill for six weeks with an irregular fever, said to be malarial. At this time she was nursing an infant one year of age. The labor had been natural, and she had a good getting up. Three years ago she had an attack of malarial fever, and at one time had rheumatism of the leg. She never had any other ailments, and was strong and hearty, and of temperate habits. The family history was good. The parents and several brothers and sisters are still living. One sister died of pneumonia; the cause of death of another is unknown.

On admission, it is noted that the patient is prostrated, and complained of chilly sensations and of nausea, and sweat profusely. The tongue was clean and moist. The bowels were loose, there being five movements in the twenty-four hours, the stools thin and greenish in color. The nausea disappeared in the course of twelve hours. There was some tenderness in the epigastrium, but none in the iliac fossa. The spleen extended in the axillary line, from the sixth rib to the margin of the ribs. There was no eruption. Both cheeks were flushed, the skin and mucous membranes were pale, the hands quite anæmic, and the body somewhat emaciated; the mind was clear. The lungs and heart were normal. A nutritious diet, with stimulants and quinia, were ordered. Five days later a cardiac murmur was detected. The general condition and symptoms were about the same. The apex-beat of the heart was in the fifth interspace, in the nipple line. The impulse was moderately feeble; there was no thrill. The pulmonary second sound was somewhat accentuated. A low-pitched, systolic murmur was heard at the apex, and transmitted into the axilla. There was no mur-

mur at the aortic orifice. The pulse was rapid, small, and feeble. There was no cough nor dyspnoea. Ulcerative endocarditis was suspected.

September 8th. It is noted that the fever has continued, in spite of the use of quinine. There were profuse sweats during the day, but not at night. The anæmic appearance of the face was marked, and the patient was evidently losing flesh and strength. The diarrhoea continued. The cardiac murmur had increased in intensity, and could be loudly heard at the angles of both scapulæ, especially on the right side. There was marked tenderness on pressure, and some pain in the third left intercostal space. At the base of the right lung, impaired resonance and fine, moist, crepitant râles were observed. A few râles were also found at the right apex. There was short, high-pitched, jerking inspiration and prolonged expiration at the right apex, and high-pitched inspiration at the left.

September 12th. Two days ago, two small, purpuric spots were observed on both upper eyelids, and to-day, hæmorrhagic infarcts are seen all over the trunk and on the upper extremities, pin-head to split-pea size, bright red in color, not disappearing on pressure. Hæmorrhages in the bulbar and palpebral conjunctivæ of both eyes, at the inner and outer canthus, were also seen. The patient was rapidly losing flesh and strength, and the sweats continued. The abdomen was distended in the epigastric and umbilical region, and a large, wavy impulse was detected in the epigastrium. Nausea and vomiting had recurred during the past five days, and the diarrhoea continued. The spleen was tender, and could be readily felt below the margin of the ribs. The pulmonary signs had disappeared. There were no cerebral symptoms. The heart's action was irregular, and the pulse small, feeble, rapid, and dicrotic. In the second interspace to the left of the sternum, a perceptible thrill was present. The systolic murmur was

not so loud at the apex as it had been. Over the third rib, a loud, booming, systolic murmur, with a "grinding" element, was heard. In the second interspace to the left of the sternum, there was heard a loud, rough, high-pitched murmur. The pulmonary second sound was muffled. The murmur over the tricuspid valve was not so distinct as over the mitral valve. There was no œdema, and the mind continued clear.

The day following there was a chill. The urine was scanty, high-colored, and contained blood and a small quantity of albumen. Blood and epithelial tube-casts were found in abundance. The chill was repeated the next day (14th). The patient was a little more drowsy, but there was no delirium. New capillary infarcts were seen about the neck. Infarcts also involved the lips and end of the tongue. The conjunctivæ were slightly icterode. For half an hour there was severe dyspnoea. The exhaustion increased, and the patient died in the early morning of September 15th.

I have here the temperature chart showing the course of the fever during the disease. As will be seen, there were marked remissions. Twice the temperature was above 105° , and on one occasion it reached 105.8° . At the same time the pulse was excessively rapid and feeble.

You will observe here again symptoms due to the general process, symptoms due to the local cardiac trouble, and symptoms due to the infarcts. The case presents a most typical example of the evolution of the clinical phenomena of malignant endocarditis.

It is of interest on account of the difficulty of diagnosis. It was at first thought possible that the case was one of malarial fever of a remittent type. The failure of large doses of quinia to control the fever, the appearance of the infarcts and the development of the cardiac murmur, led us very soon to abandon the idea

of malaria, and look upon the case as one of ulcerative endocarditis. Until the development of the hemorrhagic infarcts in the skin and the occurrence of renal emboli, there was not sufficient evidence to warrant a positive diagnosis, however. Typhoid fever was thought of. Many of the cases of malignant endocarditis which have not been regarded as cases of intermittent fever have been considered to be cases of typhoid fever. In this case there was diarrhœa, enlarged spleen, and the occurrence of fever with prostration. In other cases the typhoid symptoms are more marked than in our case, so that a mistake in diagnosis is readily made. In this case, as in most instances, the temperature was not characteristic of typhoid fever. In the latter disease, the temperature follows a certain regular course; further the abdominal symptoms are more marked than in ulcerative endocarditis, the lesions of the heart are absent, the pulse is not so frequent, the sweats are not so profuse, the hemorrhagic infarcts are wanting, and the rose-colored spots characteristic of typhoid fever are found. By bearing these points in mind a mistake is not apt to be made. A mistake is most likely to be made in those cases of typhoid fever in which the temperature range is very irregular.

There are some cases in which typhoid fever occurs in a person who already has heart disease. This may obscure the diagnosis, but the uniform character of the murmur, the absence of capillary infarcts, the absence of jaundice and the presence of marked abdominal symptoms would lead us to a correct diagnosis. A point in the diagnosis of recent malignant endocarditis from long-standing heart disease complicating typhoid or intermittent fever is, moreover, the presence of either hypertrophy or dilatation in the latter case. You may not be able to differentiate the cases from the seat or the character of the murmur, but if

these changes in the structure of the muscles were noticed, you would infer that the cardiac lesion was of long standing, and that a febrile affection had occurred in a subject of chronic heart disease.

At one time, before the cardiac symptoms appeared, it was thought that this might be a case of tuberculosis. The sweats, irregular fever, prostration and the occurrence of râles in the lungs pointed in this direction, but in our case, as in other cases of malignant endocarditis, there was wanting a symptom which is usually present in tuberculosis; that is, excessively rapid respiration. There was also absence of cause which is, however, not of much significance in acute miliary tuberculosis. The appearance of the cardiac symptoms and the peculiar range of temperature, led us to eliminate this affection.

I have already mentioned that malaria is often simulated by ulcerative endocarditis. Many cases treated as ague, have turned out to be instances of the pyæmic variety of malignant endocarditis. The presence of the germ of Laveran in the blood, would at once confirm the diagnosis of ague, or the presence of pigment in the blood and tissues would point to malaria. The cases are sometimes very difficult to settle, and due attention must be paid to their minor details.

Where a murmur develops in the course of articular rheumatism, it is sometimes difficult to decide whether it is due to a septic process or to a simple endocarditis which frequently complicates rheumatic affections. If in the course of rheumatism ulcerative endocarditis sets in, the temperature will be out of proportion to the rheumatic manifestations. The physical signs differ from those of simple endocarditis. In the latter there is a soft, blowing, low-pitched murmur which is not so widely transmitted as in the former. The murmur of simple endocarditis is persistent and of one character continually, while the murmur of malignant

endocarditis varies in seat and in intensity from day to day. One day it may appear to be limited to the mitral valve, the next day, to the aortic valve. This variation depends upon the amount of exudation present, and whether or not it is set free in the course of the disease. If a large mass of vegetation disappears from the valve, the symptoms will change in character. This is not the case in simple endocarditis. Bearing in mind this difference, and remembering that in simple endocarditis, infarcts do not occur, that jaundice does not develop, and that the spleen does not become enlarged, the differential diagnosis can usually be made.

The case which I now bring before you is one of rheumatism extending over a long period of time, and presenting some features which might lead one to infer the occurrence of malignant endocarditis, but there are some other features which negative that idea entirely. The points suggesting malignant endocarditis are the irregular temperature, as is seen from the chart, the long continuance of the case, the frequent exacerbations after a short period of normal temperature and the presence of cardiac lesion. There are, however, two or three points which are in opposition to this view. In the first place, each exacerbation of fever occurred at a time when there was a fresh attack of joint pain. During the past two weeks, the joint symptoms have been limited to the knee, and have not been very marked. The pain complained of is, I think, at present largely of an hysterical nature. The patient has been under observation six weeks. There is present a murmur which during the whole time that the patient has been under observation has not changed its character. The murmur is limited to the mitral valve, is low pitched and soft and blowing in character. These are the characters of the murmur of recent endocarditis. Moreover, the murmur is not accompanied by the profound disturbance of circula-

tion that is found in cases of malignant endocarditis where there are large vegetations projecting into the lumen of the valves.

A method of differential diagnosis which might be of value has not been referred to. Capillary hæmorrhages are known to occur in the fundus of the eye before they appear in the superficial structures, and an examination of the eye-ground would therefore be of great service in the recognition of endocarditis.

The prognosis of malignant endocarditis is, of course, extremely grave. There are some cases which are said to have recovered, but in these cases, there is an element of doubt. It seems impossible that a mistake could be made where the local cardiac trouble, with the infarcts and the pyæmic symptoms are present. The reason that the disease has not been oftener diagnosed is because it has not been suspected.

The treatment, as will be inferred from my remarks, is unsatisfactory. In the large number of cases it can only consist in the treatment of symptoms. The presence of micrococci in this disease has only recently been demonstrated, and its septic character shown. Remedies to counteract the septic process have been administered. One case has recently been reported by Dr. Samson, in which the administration of sulpho-carbolate of soda in thirty grain doses three times a day, had been followed by cure of the patient. Apart from the administration of the sulpho-carbolates, the use of carbolic acid and the bichloride of mercuria in minute doses I believe would be valuable. Stimulants and iron in large doses, if the stomach will bear it, are indicated. It is, however, usually not possible to give iron, on account of the vomiting. The treatment of the pyrexia also requires attention. In our patient it seemed that the administration of antipyrine in five grain doses every third hour with a stimulant to prevent the depressing effects of the drug, was of advan-

tage. Certainly the temperature range was not so great after the use of this drug as before, but as we have seen from the chart of the first case, the temperature is very variable, so that it is difficult to judge as to the effect of drugs. The patient also received three drops of tincture of belladonna three times a day, for the control of the exhausting sweats. The diet was of the most nutritious and stimulating character, but as happens in most of these cases, all treatment was without avail.

Malignant endocarditis is a disease that was not recognized until within recent years. It is a rare disease. This is shown by the fact that Dr. William Osler, in a thorough search of the literature, was able to find only 209 cases. Since his admirable lectures were delivered in London two years ago, a great impetus has been given to the study of malignant endocarditis, and many cases are now recognized which before were entirely overlooked. The lines of investigation which have been pursued and which are still being pursued are in the direction of the explanation of the septic process, and the relation of malignant endocarditis to pneumonia, rheumatism and other infectious diseases.